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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,943	08/21/2006	Brian E. Jones	GC796-2-US	7104

7590 08/19/2008

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
08/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,943	JONES ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-21,25-28 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-21, 25-28, and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-21, 25-28, and 30 are currently pending.

In response to a previous Office action, a non-final action (mailed on November 16, 2007), Applicants filed a response and amendment received on May 15, 2008, amending claims 1-3, 5, 7-10, and 15-16, and cancelling claims 6, 22-24, and 29-33 is acknowledged.

Claims 1-5, 7-21, 25-28 and 30 are under consideration and are present for examination.

Applicants' arguments filed on May 15, 2008, have been fully considered but are not deemed persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Maintained-Claim Objections

Previous objection of Claim 3 in the recitation "isolated nucleotide" is maintained. The objection can be overcome by changing the phrase "isolated polynucleotide" Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previous rejection of Claim 2 under 35 U.S.C. 112, first paragraph, on written description requirement is maintained.

Claim 2 is directed to any polynucleotide which hybridizes with recited hybridizing conditions followed by washing in 0.1 X SSPE and 0.5% SDS at 42oC to SEQ ID NO: 1,

wherein the polynucleotide is selected from the group mRNA, DNA, cDNA, or genomic DNA, wherein said polynucleotide encoding an enzyme having cellulase activity, wherein the enzyme is isolated from a *Trichoderma reesei.*

Applicants argue that Applicants have amended claims 1-3, 7-10 and 16 rendering this rejection moot and withdrawal of the rejection.

Applicant's amendments to claims and arguments have been fully considered but are not deemed persuasive to overcome the rejection on written description issues.

Examiner acknowledges amendment to the claims, however the amendment does not give enough structural feature of any or all polynucleotides, which will remain bound after washing at 42oC to SEQ ID NO: 2, wherein washing at 42oC is not enough high stringent washing condition that will allow many nucleic acid fragments to remain bound to the target sequence of SEQ ID NO: 2 that is required for fulfilling written description requirements.

The specification does not contain any disclosure of the structures of all DNAs which will remain hybridized to SEQ ID NO: 1 or 2 after washing at 42oC. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only two representative species of the claimed genus (DNA) i.e. SEQ ID NO: 1 and 2, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Therefore, the rejection is maintained.

Previous rejection of Claims 1-5, 7-21, 25-28 and 30 under 35 U.S.C. 112, first paragraph on scope of enablement is maintained. This rejection has been discussed at length in the previous

office action. The rejection is maintained for the following reasons.

The specification, while being enabling for a nucleic acid sequence of SEQ ID NO: 1 or 2 encoding polypeptide of SEQ ID NO: 3 having cellulase activity isolated from Bacillus agaradhaerens, an expression vector, transformed host cell comprising said nucleic acid sequence, a detergent composition comprising said polypeptide and a method of treating wood pulp with said cellulase polypeptide, does not reasonably provide enablement for any nucleic acid sequence which is 85-90% identical to SEQ ID NO: 1 or 2 or any nucleic acid sequence which remain hybridized after washing at recited conditions including 42oC to SEQ ID NO: 1 or 2 or any polypeptide encoded by SEQ ID NO: 1 or 2, which is 85-90% identical to SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, **to make and use** the invention commensurate in scope with these claims.

Applicants argue that Applicants have amended claims 1-3, 7-10 and 16 rendering this rejection moot, and applicants submit that the claims overcome this rejection under 35 USC §112.

Applicant's amendments to the claims and arguments have been fully considered but are not deemed persuasive to overcome the rejection on scope of enablement issues.

Claims 1-21, 25-28 and 30 are so broad as to encompass any nucleic acid sequence which is 85-90% identical to SEQ ID NO: 1 or 2 or any nucleic acid sequence which remain hybridized after washing at recited conditions including 42oC to SEQ ID NO: 1 or 2 or any polypeptide encoded by SEQ ID NO: 1 or 2, which is 85-90% identical to SEQ ID NO: 3, i.e. 10-15% non-

identity (i.e. 58-87 altered amino acids out of 581 amino acids), which encompasses many mutants, and variants as well as many nucleic acid fragments due to 85-90% identity to SEQ ID NO: 1 and 2 as well as hybridizing washing conditions at 42oC.

The claims are still broad in the context of any DNA or encoding protein which is 85-90% identity to SEQ ID NO: 1 or 2 (for DNA) and SEQ ID NO: 3 (for protein) as well as any DNA fragment which will remain bound after washing at 42oC, wherein washing at 42oC is not enough high stringent washing condition that will allow many nucleic acid fragments to remain bound to the sequence of SEQ ID NO: 2.

The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the extremely large number of cellulase gene encoding cellulase protein including many mutants and fragments and variants broadly encompassed by the claims. Since the nucleotide sequence of polynucleotide determines the encoded amino acid sequence of a protein which in turn determines structural and functional properties of said encoded proteins, predictability of which changes can be tolerated in said nucleotide sequence and in turn in the encoded a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which nucleotide affect what which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only two nucleic acid sequences and a single amino acid sequence having cellulase activity to make the composition and used for treating wood pulp.

While methods to produce a polypeptide or its variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. With only the limited guidance provided by the specification one of ordinary skill would be reduced to the necessity of producing and testing virtually all of the possibilities. This would clearly constitute **undue** experimentation. Guo et al. teach that the percentage of random single substitution mutations which inactivate a protein for the protein 3-methyladenine DNA glycosylase is 34% and that this number appears to be consistent with other studies in other proteins as well. Guo et al. further show in Table 1 that the percentage of active mutants for multiple mutants appears to be exponentially related to this by the simple formula $(.66)^x$ X 100% where x is the number of mutations introduced. Applying this estimate to the instant protein 85% identity allows up to 87 mutations within the 581 amino acids of SEQ ID NO: 3 and thus only (.66)87 X 100% or 2.0 x 10^{-14}% of random mutants having 85% identity would be active (i.e. 1 in several hundred trillions). Similarly, at 95% identity 5.8 x 10^{-4}% would be active (1 in 171,000). Current techniques (i.e., high throughput mutagenesis and screening techniques) in the art would allow for finding a few active mutants within few hundred thousand inactive mutants as is the case for the claims limited to 95% identity (despite even this being an enormous quantity of experimentation that would take a very long time to accomplish) but finding a few mutants within several hundred trillion or more as in the claims to 85% identity would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance

with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claim 15 under 35 U.S.C. 102(b) as being anticipated by Ahsan et al. (Cloning, DNA sequencing, and expression of the gene encoding Clostridium thermocellum cellulase CelJ, the largest catalytic component of the cellulosome, J Bacteriol. 1996 Oct;178(19):5732-40) is maintained. Instant claim is directed to a substantially purified cellulase or an active fragment of SEQ ID NO: 3. Ahsan et al. disclose a cellulase, which is 26.2% identical to SEQ ID NO: 3 (see attached sequence alignment) having cellulase activity. Ahsan et al. also disclose purification of said cellulase. Therefore, Ahsan et al. anticipate claim 15 of the instant application.

Applicants argue that the cellulase disclosed by Ahsan is only 26.2% identical to SEQ ID NO:3. This identity fails to meet the lowest identity (i.e., 85% identity) required by the claim (subsections a- d). Subsection e requires that the fragment retain cellulose activity. Although there is no identity requirement provided, Applicants submit that the biologically active fragment of SEQ ID NO:3 would not have the sequence found in Ahsan. Conversely, the cellulase

disclosed by Ahsan would not have the sequence of a biologically active fragment of SEQ ID NO:3.

Applicant's amendments to the claims and arguments have been fully considered but are not deemed persuasive to overcome the rejection on anticipation issue. Claim 15, part (e) recites "a biologically active fragment of SEQ ID NO: 3" in terms of cellulase activity as biological activity of said fragment. Ahsan et al. indeed disclose a cellulase (same biological activity as instant application), which is 26.2% identical (best local similarity) to SEQ ID NO: 3 (see attached sequence alignment) having cellulase activity. Therefore, the polypeptide of Ahsan et al. meets the scope of the claim as written, i.e. claim requires "a biologically active fragment of SEQ ID NO: 3" and Ahsan et al. teach a polypeptide within the scope of the claim as written. Therefore, the rejection is maintained.

Withdrawn-Claim Rejections - 35 USC § 103

Previous rejection of Claims 5, 14 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jung et al. (DNA sequences and expression in Streptomyces lividans of an exoglucanase gene and an endoglucanase gene from Thermomonospora fusca. [Appl Environ Microbiol. 1993 Sep;59(9):3032-43)] as applied to claims 1-5, 7-9, 11-13, 17, and 19-21, and further in view of Godbole et al. (Cloning and expression of Trichoderma reesei cellobiohydrolase I in Pichia pastoris, Biotechnol Prog. 1999 Sep-Oct;15(5):828-33) is withdrawn in view of applicants amendment of claims 1, 3, 5, 7-10, 15-16. Indeed, the cited references do not make obvious the polynucleotide encoding a cellulase from Bacillus source,

which is 85% identical to SEQ ID NO: 3, host cell and method of making the cellulase by using the polynucleotide.

Conclusion

Status of the claims:

Claims 1-5, 7-21, 25-28, and 30 are pending.

Claims 1-5, 7-21, 25-28, and 30 are rejected.

No claims are allowed.

Applicants must respond to the objections/rejections in each of the sections in this Office action to be fully responsive in prosecution. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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